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The NIH CATALYST

A PUBLICATION FOR NIH INTRAMURAL SCIENTISTS

NATIONAL INSTITUTES OF HEALTH ■ OFFICE OF THE DIRECTOR ■ VOLUME 10, ISSUE 4 ■ JULY–AUGUST 2002

WILLIAM PAUL: 'LIFETIME' ACHIEVEMENT A WORK IN PROGRESS

by Masashi Rotte

In the four decades between the 1963 publication of his first paper—"Relationship of gamma globulin to the fibrils of secondary human amyloid"—and his seven contributions to the literature thus far in 2002 (two published, three in press, two submitted) that address the differentiation of mem-ory T cells and the activities of inter-leukin-4 (IL-4), there has occurred what William Paul calls a "revolution" in the field of immunology.

He doesn't credit his own role in fomenting that revolution—but his peers are well aware of it. This past spring, he received the American Association of Immunologists' 2002 Lifetime Achievement Award. *The NIH Catalyst* interviewed him shortly after.

Masashi Rotte

William Paul

Asked to list some of the achievements especially pleasing to him, Paul cited the "wonderful colleagues" that had been his trainees and "a lot of the research that has been done here." Much of that research has involved IL-4.

Paul discovered and purified IL-4, characterized and traced the signaling mechanism of the IL-4 receptor, and elucidated the regulation of IL-4 production. He demonstrated the role of IL-4 in the production of IgE antibodies, the regulation of allergic inflammatory diseases, and the polarization of T-cell responses to the

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Proposed Homeland Security Department Would Work with DHHS

NIAID'S BIODEFENSE RESEARCH AGENDA IN ACTION, CITED AS CRUCIAL TO CIVILIAN ANTI-BIOTERROR EFFORTS

by Fran Pollner

Barely three weeks into his tenure as NIH director, Elias Zerhouni presided over his first meeting of the Advisory Committee to the Director (ACD) June 6, where he heard a report on the NIAID "Strategic Plan for Counter-Bioterrorism Research." That evening, President George W. Bush went on national television to propose a new cabinet-level Department of Homeland Security—a department that, as proposed, would assume authority over the biodefense-related research of NIH [see "From the Homeland Security Act of 2002," page 5].

An inkling of what was to come was contained in a small news release handed to Zerhouni just as Jack Killen, NIAID assistant director for biodefense research, was to brief the new NIH director and the ACD on the status and scope of NIAID's biodefense research agenda. Zerhouni read the one-sentence news release on the proposed new department, which did not overtly suggest that NIH might be affected, and that possibility was not discussed at the ACD meeting.

The NIAID "strategic plan" was also addressed in the kickoff speech of the NIH Health and Safety Expo a few days later—when the implications of the administration proposal could only be guessed at; see below.

The president's proposal was later sent to Congress as H.R. 5005; hearings before relevant House and Senate committees, held in June and July, were peppered with the testimony of non-NIH witnesses advising the legislators that the president's objectives would best be served by retaining control over NIH biodefense-related research within the Department of Health and Human Services, with the proposed Department of Homeland Security having overall guidance and coordinating functions [see "Congress Gets into the Homeland Security Act," page 5]. In early July, at his first press conference with the print media, Zerhouni addressed the issue [see page 4].

NIAID Strategies

The NIAID biodefense focus, Killen told the ACD, is on infectious diseases and toxins unleashed on a civilian population, a cohort considerably more vast and diverse than the military population. Unlike the military situation, civilian attacks would be unexpected and require rapid diagnostic and therapeutic responses in many different settings.

Targeted for immediate intensive research are those organisms designated Category A by the Centers for Disease Control—organisms deemed to pose the

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Special Interest Groups: An Assessment

Michael Gottesman

The concept of special interest groups (SIGs) at NIH was formalized eight years ago, shortly after I became DDIR and with the strong encouragement of Harold Varmus, who had just assumed the directorship of NIH.

The idea grew out of the important contributions made by pre-existing grassroots trans-NIH scientific groups such as the Lambda Lunch (bacterial and phage genetics), structural biology, glycobiology, and immunology. Similar in concept was a major recommendation of the 1992 Klausner committee report on intramural administration that suggested that the creation of "faculties" at NIH would give scientists a stronger voice in decision-making about science issues at NIH.

We started with six cross-cutting SIGs (structural biology, immunology, cell biology, molecular biology and biochemistry, neurobiology, and genetics) and added clinical research shortly thereafter. Small working groups of scientists with similar interests driven by specific molecules, methodology, and model organisms sprang up quickly, and this current issue of *The NIH Catalyst* lists a total of 89 SIGs.

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Although the level of activity of these groups varies, many have a regular seminar series and occasional workshops, and they provide a support group for trainees and new scientists entering a particular research area.

The Office of Intramural Research and the Office of the Director, NIH, support websites and cost of conference facilities and also have a small budget to help defray the cost of bringing speakers to a few special SIG-sponsored workshops.

In addition, the SIGs assist with the Research Festival, nominate speakers for the NIH Director's Wednesday Afternoon Lecture Series, and contribute in a major way to the high quality of speakers who come to NIH.

Overall, my sense is that the SIGs have been a successful experiment, leading to collaborations across institutes and giving scientists a stronger voice in obtaining resources and recruiting colleagues to the intramural program.

Our tenure-track scientists have told me how much they appreciate finding like-minded colleagues quickly after their arrival at NIH, and I frequently use the SIGs as a source of advice when I am looking for experts in a specific scientific area. Good suggestions about how to do things better at NIH have come from the SIGs, whose chairs I meet with annually.

How can we strengthen the effectiveness and influence of the SIGs at the NIH? Our new director, Elias Zerhouni, has challenged our scientific directors to help define biomedical research bottlenecks and knowledge gaps that can be filled by intramural research activities and infrastructure. Can we use the existing SIGs more effectively to identify areas of research and infrastructure requirements in which the intramural program should be taking a lead?

Current exciting opportunities in neuroscience, functional imaging, structural biology, and immunology, including vaccine development, among many others, have benefited from the interactions between the scientific leadership at NIH and the SIGs. As new areas of research develop (for example, stem cell biology), can we use the SIGs to mobilize interest, define needed resources, and provide direction in support of such activities?

Historically, our SIGs and other trans-NIH groups have provided a useful focus for concentrating talent and resources on problems of importance to the scientific community at large.

For example, the development of recombinant DNA technology was given a boost by the concentration of phage and bacterial geneticists at NIH; advances in HIV research benefited from the large concentration of retrovirologists and HIV researchers at NIH; trans-NIH imaging activities have made us a leader in this area; array users have helped spread this research tool quickly in the Intramural Research Program.

I would appreciate feedback on how the SIGs can be even more effective than they are now, especially in the development of new research areas. As always, I welcome and encourage your thoughts on this issue.

—Michael Gottesman
Deputy Director for Intramural Research

Introductions All Around: New Director Meets His Outside Advisors . . .

by Fran Pollner

Bill Branson

On the Job: *Elias Zerhouni (center) enjoyed his inaugural meeting with his committee of outside advisors. Insiders Ruth Kirschstein (left), NIH deputy director, and Michael Gottesman (right), deputy director for intramural research, enjoyed it as well.*

Elias Zerhouni met with his Advisory Committee to the Director (ACD) of NIH for the first time on June 6. Except for the passing of the gavel from Ruth Kirschstein (once again NIH deputy director) to the new director, the agenda for the meeting had been set long before the date and before it was known that the vacancy for the top spot at NIH would be filled by the time of the meeting.

When Zerhouni commented on how much fun the meeting was—what with jovial introductions, a comical exchange between himself and ACD member and former boss Bill Brody (president of the Johns Hopkins University), and a delightful performance by students from the CityLab of Boston University School of Medicine—ACD members hastened to disabuse him of the notion that the meetings were always so appealing.

But it was too late. The camaraderie and collegiality had already been established.

From his opening remark that he was "honored and excited to be here" and impressed by the composition of his advisory committee, Zerhouni made it clear that he had no reservations about having taken on the responsibilities of the NIH director—even when he joked that were it not for Ruth Kirschstein, there were a few days he might have left for the evening and not returned. He mentioned that during his time at Hopkins he'd been on the receiving end of other job offers that he'd declined rather quickly, but that the one job he always knew he wouldn't hesitate to accept would be the one he now had.

In office scarcely more than two weeks, Zerhouni had not yet absorbed everything there was to know about the internal workings of NIH and its relations with the political powers that be, but, he said, he had discerned "one big difference between my job at Hopkins and my job here—there I did four jobs for the price of one; here I have one job and so many bosses I'm not done counting. . . ."

He had also become aware during his first two weeks at NIH and during the nomination process before that the "first and foremost" issue on the mind of every senator and congressman with whom he spoke was the need for a clear return on the doubling of the NIH budget. "There is a huge cry for accountability and transparency . . . and the translation of discovery into tangible benefits."

That expectation is fueled by a somewhat mistaken comparison between landing on the moon and curing disease, he said. The former was a technological challenge based on known laws of physics and gravity—and the presidential promise of a moonshot within 10 years was therefore realistic. But the endpoints and signposts along the way are not so well defined in biomedical science, he said. "We need to communicate to the public that we face a knowledge challenge."

Meeting that challenge by bringing the tools and mysteries of biomedical research into the lives of students in grades 7 through 12 is the essence of the CityLab program, a project funded by the NCRR Science Education Partnership Award and the Howard Hughes Medical Institute. The program brings students into Boston University labs or brings a mobile lab to the students on their own turf. Zerhouni appeared captivated by a well-choreographed presentation by about a dozen CityLab students and after they had finished asked for a show of hands: "How many of you will be around this table in 25 years?" All hands went up. "Please," Zerhouni requested, "leave your names here, so we may follow your progress. I would love to do that."

He recalled that he was eight years old when his father, a teacher of math and science, set him on his career path: "He showed me experiments with magnesium and oxygen, and there was this big flash—and that's what got me!" ■

Bill Branson

Elias Zerhouni

. . . and the SDs

by Celia Hooper

Meeting with the scientific directors of the NIH intramural research programs a month after beginning work here, NIH's new director talked a little, listened a lot, and passed out assignments.

Within a week, Elias Zerhouni gently requested, the SDs should send him descriptions of three areas in their institutes' portfolios that represented unique contributions to biomedical research. He also urged them to form a think tank to identify research bottlenecks.

The goal of the assignments, he said, was to strengthen his hand "in conveying a vision of the future of biomedical research and the knowledge gaps that must be filled."

Zerhouni said he sees an increasing need for a "big picture" analysis of bottlenecks in research and a team approach in its conduct. "There is a need for convergence of scientists and disciplines—a thematic approach to management and in the way we describe the work," to Congress and others, internally and externally, Zerhouni told the SDs. "It is much easier to convey the science as a theme than as part of an organizational chart."

He noted that talks with members of Congress before his confirmation hearing made him acutely aware that NIH will be held accountable for results from the fast pace of funding increase it has enjoyed over the past four years.

Scientists need to educate patient-advocacy and lobbying groups to appreciate the difference between "science-based funding and funding-based science," Zerhouni advised. His approach to the earmarking issue is for NIH "to be utterly transparent about the way we decide which science to pursue."

The scientific community also has to be mindful that research funding is not independent of macroeconomic issues, which will need to be addressed in any cogent argument in support of research.

Zerhouni made clear that he relishes being at NIH. After touring some of NIH's new research buildings, including animal and clinical imaging facilities, he said he was amazed at the progress. Calling the intramural research program "the best in the world, second to none," Zerhouni then threw down his own gauntlet: "I want to make it better." ■

NIAID's Biodefense Research Agenda

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greatest bioterror threat by virtue of their infectiousness and lethality: anthrax, smallpox, botulism, plague, tularemia, and viral hemorrhagic fevers.

The NIAID plan covers intensive study of these agents, including genome sequencing, and of specific and nonspecific host defenses against them, as well as expansion of research capacity—training new investigators in the field, establishing a reagent repository, and building BSL-3/4 facilities at intramural and extramural sites. The extramural sites, Killen said, will be chosen competitively to form regional Centers of Excellence for Bioterrorism and Emerging Diseases Research.

He emphasized that the NIAID bioterror defense program "is based on the concept that bioterror is a subset of the greater problem of emerging and reemerging diseases." He noted that over the last decade or so, about 30 different organisms have reared their problematic heads around the world.

He also provided a rundown of the president's FY2003 budget request—delivered at the beginning of the year—that includes $37.7 billion for homeland security, of which $5.9 billion would go toward defending against bioterrorism. The NIH biodefense budget, he said, would increase from $274.5 million this year to $1.75 billion in 2003. The construction of research facilities would account for about $520 million; about $440 million would go toward basic research on agents of bioterrorism; and about $590 million would fund development and testing of therapeutic drugs, vaccines, and diagnostics. The request projects out to 2006, with construction money falling over the years as clinical research and development outlays grow.

Questions having largely to do with the security aspects of the NIAID program dominated the discussion after Killen's presentation. Would the biosafety features of the new laboratory facilities serve to keep people out as well as keep pathogens in? Would there be a special vetting process for both intramural and extramural investigators involved in the program? Would there be restrictions on publishing the results of research?

NIH philosophy, Killen noted, has always been that information should be placed in the public realm in as complete and timely a manner as possible. "That said," he continued, "there probably will be some things that are better not placed in the public realm. We have to feel our way into this, beginning from a position of openness." As for the vetting of investigators, he guessed that there "would need to be some restrictions on those with direct access to [potential bioterror] agents—probably related to a security clearance process. Standards are being developed—and quickly," he said.

That night, President Bush made his announcement, and the following day, it was reported that among those operations that would be "absorbed" by the proposed Department of Homeland Security were "HHS civilian biodefense research programs" involving 150 full-time employees and $1.9 billion. NIAID spokespersons contacted by the *Catalyst* said they did not know how or whether the president's reorganization plan would affect the NIAID biodefense research program but that they'd "continue doing what we're doing."

NIAID in Action

Several days later, on June 11, Carole Heilman, director of the NIAID Microbiology and Infectious Diseases division, gave her scheduled talk on "NIAID BioDefense: The Response and Role of NIH" to keynote the NIH Health and Safety Expo held that day.

She presented an overview much like Killen had, but when she delineated the spokes of the overall HHS biodefense program—CDC surveillance and stockpiling of vaccines and antimicrobials; NIH basic research and medical interventions; FDA regulatory approval of vaccines, therapeutics, and diagnostics; and OEP (Office of Emergency Preparedness) resource mobilization and local-federal coordination—she issued a caveat: "This is how we look today. Indeed, I'm not sure if this is how we'll look in a little while."

Fran Pollner

Carole Heilman (right) answers more questions following her talk on the NIAID biodefense research program

Heilman proceeded to summarize the sorts of biodefense activities in which various NIH institutes are currently engaged: NIGMS epidemic modeling, NIEHS environmental assessment of contamination, and NINR and NIMH examination of post-traumatic stress sequelae, in addition to the NIAID focus on pathogens and immune response.

Thus far, she said, the NIH response to the precipitous bioterror threat unleashed in the fall of 2001 has yielded a "remarkable [array of] accomplishments in record time." Among the activities she noted were the following:

- Smallpox vaccine dilution studies: A clinical trial involving 680 healthy adults established that existing stocks of smallpox vaccine are effective at 1:5 and 1:10 dilutions.
- Smallpox vaccine development: In the face of insufficient stores of vaccinia immunoglobulin to protect immunocompromised populations at risk of dis-

Zerhouni: NIAID's Momentum To Continue

Asked where the Administration blueprint to establish a Department of Homeland Security would place the decision-making authority in awarding NIH biodefense-related research, NIH Director Elias Zerhouni responded, "We've already implemented a strategic plan [the NIAID Strategic Plan for Counter-Bioterrorism Research], and we will continue [to award grants]. We will also continue to implement the construction of needed facilities."

In his first press conference with the print media, held in his NIH office July 2, Zerhouni emphasized the need to "continue the momentum" generated by NIAID. Asked what it means for NIH to be a contractor to a homeland defense agency, Zerhouni noted that deciding how best to implement a biodefense research program requires an analysis that has yet to be undertaken. Until that has been achieved, he said, the "mechanism to have NIH continue" on its current path by having the new department coordinate policy and "contract back" the funds to NIAID to execute the program is "probably the best strategy" given the current state of knowledge.

He noted that biodefense "is not necessarily driven just by bioterrorism. We need to defend against naturally occurring organisms and to establish an infrastructure responsive to the emergence of new threats, whether man-made or not, and to reemerging infections." That model, he said, is not easily achieved. He did note, however, that "NIAID has developed quite an infrastructure." ■

seminated vaccinia, testing is underway of a less reactogenic smallpox vaccine based on modified vaccinia Ankara.

- Antiviral drug development: In testing the repertoire of antiviral drugs against both vaccinia and smallpox, cidofovir has emerged as a base from which to develop effective therapies.
- Anthrax pathogenesis studies: Three linked mechanisms of cell entry, any one of which can be modified to block infection, have been discovered.
- In collaboration with the Navy, genomic sequencing of *Bacillus anthracis* has been accelerated.
- In collaboration with the National Science Foundation and The Institute for Genomic Research, studies have yielded possible forensic markers to identify sources of *B. anthracis*.
- In collaboration with the military, studies are underway to develop a civilian alternative to the military's anthrax vaccine, which requires six injections over 18 months, a regimen that would not work in a bioterror setting.
- Ongoing VRC studies are untangling the complexities of the Ebola virus' life cycle, leading to the development of candidate vaccines.
- Along the biodefense product pipeline, NIAID is geared up to travel from pathogen to product through the stages of basic research, target identification, preclinical development, and clinical evaluation. RO1 and PO1 grants are going out in FY2003 for basic research in pathogen replication and pathogenesis, animal models of infection, and host and innate immune response.

Industry collaborations are being sought for preclinical development and to expand GMP/GLP facilities for manufacturing vaccines and drugs. HHS has asked for speed in developing one particular anti-anthrax product—recombinant protective antigen, or rPA.

- NIAID has also expanded clinical studies to examine mucosal immunity, food- and water-borne infections, and respiratory infections; international sites are being developed.
- In addition to the newly conceived Regional Centers of Excellence for Biodefense and Emerging Infectious Disease Research, FY2003 money is also targeted to the establishment of Centers of Human Immunology to explore how to manipulate the immune response to selectively and specifically respond to unknown pathogens. ■

Congress Gets into the (Homeland Security) Act

Introduced into the House on June 24, the Administration's proposal to establish the Department of Homeland Security, was referred to a dozen different congressional committees with jurisdiction. Several held hearings the last week in June and in early July; those conducted in the House Energy and Commerce Subcommittee on Oversight and Investigation and the Senate Governmental Affairs Committee focused particularly on those sections of the proposal dealing with the transfer of programs or authority over programs from the Department of Health and Human Services to the Department of Homeland Security. Sen. Joe Lieberman (D-Conn.), the chairman of the Senate panel, had authored an earlier bill to create a national homeland security department that calls for many of the changes adopted in the Administration proposal but does not alter HHS authorities. It is his committee that will prepare and shepherd the Senate version of the Administration bill through the legislative process. "I want to explore the wisdom of [the Administration] approach—how and if it would work," he said.

Witnesses addressing the NIH civilian biodefense research program cautioned that shifting control to the new department might compromise scientific expertise and public health objectives. Gail Cassell, vice president of scientific affairs and Distinguished Lilly Research Scholar for Infectious Diseases of Eli Lilly and Company, Indianapolis, emphasized the need for "excellent science based upon peer review and merit" and advised that "NIH/NIAID is uniquely positioned" to lead a biodefense effort that aligns government, academia, and industry.

Ronald Atlas, president-elect of the American Society for Microbiology (ASM), detailed the "accelerated basic and clinical research related to bioterrorism" already undertaken by NIH, in particular NIAID. "This acceleration has occurred across the spectrum of scientific activities from basic research in microbial biology to the development of vaccines and therapeutics to research related to diagnostic systems. It is critical that this work continue to develop rapidly and efficiently . . ." To best achieve the Administration's goal of civilian biodefense, he said, the "ASM suggests reversing the responsibilities identified in Section 303(a)(2) of the Administration's Bill [see box below]."

In marking up the bill July 11, the full Energy and Commerce Committee, chaired by W. J. "Billy" Tauzin (R-La.), amended the language of the relevant sections to conform to Atlas' suggestion. More hearings before a specially convened House Select Committee on Homeland Security were scheduled at *Catalyst* press time. Members of both houses vowed to complete their versions of the legislation before the August recess. For full text of witness testimony before House and Senate committees and for access to videocasts of hearings, visit

<http://energycommerce.house.gov/> and **<http://www.senate.gov/%7Egov_affairs/hearings.htm>**.

To track the activities of the House Select Committee on Homeland Security, go to **<http://hsc.house.gov/>**.

From the Homeland Security Act of 2002

The following is part of the text of "Title III—Chemical, Biological, Radiological, and Nuclear Countermeasures. Sec. 303: Conduct of Certain Public Health-Related Activities."

(a)(1) Except as the President may otherwise direct, the Secretary [of Homeland Security] shall carry out his civilian human health-related biological, biomedical, and infectious disease defense research and development (including vaccine research and development) responsibilities through the Department of Health and Human Services (including the Public Health Service), under agreements with the Secretary of Health and Human Services, and may transfer funds to him in connection with such agreements.

(2) With respect to any responsibilities carried out through the Department of Health and Human Services under this subsection, the Secretary, in consultation with the Secretary of Health and Human Services, shall have the authority to establish the research and development program, including the setting of priorities.

The following is part of the "Analysis" of "Section 303: Conduct of Certain Public Health-Related Activities."

This section requires the secretary of Homeland Security to carry out his civilian human health-related biological, biomedical, and infectious disease defense research and development responsibilities through agreements with the Department of Health and Human Services unless the President otherwise directs, and gives the Secretary specific transfer authority to fund such agreements. In carrying out these responsibilities, however, the Secretary retains full authority to establish the research and development program, including the setting of priorities. The section also gives the Secretary specific authority to fund other research and development projects that he elects to carry out through the Department of Health and Human Services or other federal agencies.

The entire text of the Homeland Security Act of 2002 can be found at **<http://www.whitehouse.gov/deptofhomeland/bill/index.html#1>**.

An analysis of the act can be found at **<http://www.whitehouse.gov/deptofhomeland/analysis/index.html>**.

William Paul
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Th2 type. He elucidate how T lymphocytes recognize and respond to antigen and how B lymphocytes develop and are activated.

Paul began his research career as a clinical associate in the NCI Endocrinology Branch from 1962 to 1964. He returned to NIH in 1968 as a principal investigator in the NIAID Laboratory of Immunology and became chief of that lab in 1970, a position he holds to this day.

From 1994 to 1997, he was also director of the Office of AIDS Research—in which capacity he was instrumental in advancing the establishment of the Vaccine Research Center (VRC). He has authored more than 520 papers and edited more than 30 books.

Q: How has immunology changed in the 30-plus years that you've been chief of the Laboratory of Immunology?

PAUL: Basic immunology has lived through a complete revolution in the past 30 years. Immunology in 1970 and immunology in 2002 are completely different beasts. In 1970 we didn't have any of the cellular or molecular understanding of immunity we have now—people were still struggling over how many immunoglobulin genes there were. The recognition that there were T cells and B cells came only in the late '60s. The field has been transformed by improved understanding of the mechanism of immunoglobulin diversification, the whole concept of a T-cell receptor, the role of major histocompatibility complex, and the recognition of different subsets of lymphocytes.

Q: How have these findings affected public health?

PAUL: Public health changes are always much slower than scientific discoveries, but one great contribution of immunology to public health lies in vaccine biology. The old paradigm for vaccine generation was to look for the immunogen that evoked an immune response in a person who recovered from the disease. You would then try to use that information as a guide to choosing the immunogen to make your vaccine.

We now know that certain types of oligomers interact with specific receptors to turn on the immune system and that activated dendritic cells and macrophages make interleukin-12 and other co-stimulants. These types of discoveries combined with improved understanding of T- and B-cell collaboration have led to the development of better vaccines. For example, work done here at NIH [by NICHD's John Robbins and Rachel Schneerson; see "NICHD Scientists Garner 1996 Lasker Award," *The NIH Catalyst*, November–December 1996, page 15] demonstrated that the conjugation of the capsular polysaccharide of *Haemophilus influenzae* type B (Hib) to an appropriate protein could make a superior immunogen and an improved vaccine. The development of such conjugate vaccines was a great step forward in rational vaccine design; the Hib conjugate vaccine basically eliminated *H. influenzae* infection in infants in the United States. This was the principal cause of childhood meningitis and also an enormous cause of mental retardation.

Interventions in autoimmune disease are probably where you see the greatest impact of knowledge gained about immune responses. Therapies for autoimmune disease based on understanding of whole cytokine networks are coming forward. Introduction of treatment for rheumatoid arthritis based on blocking certain cytokines such as tumor necrosis factor–α is an example of the impact this new knowledge is having.

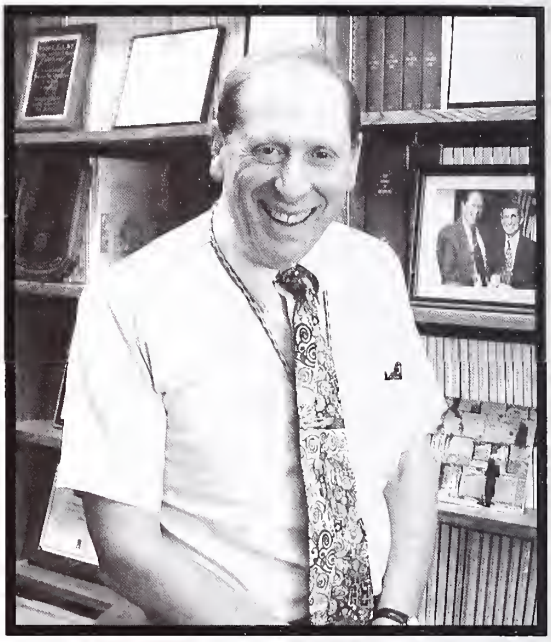
Q: What are some of the important questions immunologists need to answer in the future?

PAUL: The only way to answer that is to tell you what people are doing—and one can perhaps predict what should be done—but, generally speaking, predictions are chiefly useful for entertainment afterwards.

It seems to me that we have to learn how persistent infection is able to evoke a continuously effective state of immunity and mimic that with nonliving or engineered immunogens.

I don't think we really understand prime-boost: Why does vaccination with a DNA vaccine followed by an adenovirus or a poxvirus boost work better than DNA followed by DNA? I don't think we understand that.

Right now we understand many of the individual pathways and mechanisms of the immune system in some detail, but our understanding of how they are integrated into a fully functioning immune system is quite poor. Ideally, we would like to predict the outcome of any perturbation to the system, but we need to develop tools to understand on a quantitative basis the working dynamics and interactions of the individual components. We also need to advance ways to handle the immense amount of information we have. I think there's going to be a big emphasis on biomathematics.



Masashi Rotte

William Paul

Q: How can the Human Genome Project be used to advance immunology?

PAUL: There is enormous information to be extracted about the structure of genes that in principal may tell you something about the behavior of systems. What we want is to learn how all the components of the system work together. What do individual cells do, what determines their behavior, and how do the cells integrate various signals? That will be the basis for rational target selection in developing drugs to treat complex diseases.

Q: How has NIH changed since you first started here?

PAUL: It's a much more complex institution today, but some of the key elements have remained. Attitudes toward research have not changed. NIH is fundamentally a data-driven institution with a very high standard of scientific inquiry. The intramural research program has a real devotion to understanding and to [solving] problems of importance to human biology.

There is a real sense of community and of discovery amongst people here.

There is a much greater feeling, I think, of collegiality and cooperation than at other places where there is a lot of competition for funding.

The Immunology Interest Group (IIG), for example, is an outgrowth of the previously informal NIH immunology community. It has been very collegial since the first day I came here. There's been lots of collaboration. Even when people aren't collaborating, the interactions have been just terrific. The administration has been very sensitive to the need to provide scientists the freedom to pursue important research.

NIH has always had a substantial presence of non-US scientists, but now the mix and the places people come from are much wider. There are all sorts of enormously intelligent people that come from all sorts of backgrounds, and this is a great advantage. At one time, the physician's draft was a tool to get terrific people. We are all happy there is no draft anymore, and now we draw on all sorts of mechanisms to get our superb scientists.

Q: How has the increase in government funding to NIH affected intramural research?

PAUL: During the doubling of the NIH budget, the intramural budgets have not gone up so much; they've been relatively modest compared to the overall growth in NIH funding, most of which has been extramural.

Nevertheless, we've had the good fortune to see a lot of new construction on campus that makes up a long-standing deficit of growth in terms of physical plant. It's been very much needed and is very important to the future of NIH.

But one great thing about this institution is that the limiting step is not the battle to obtain resources to undertake an experiment; it's one's ability to come up with creative ideas to carry it out. This freedom really gives the scientist the opportunity to put an idea to the test. We're very fortunate that we don't spend the vast majority of our time trying to raise money. It's a great advantage—and a great responsibility.

Q: You had a lot of influence in getting the Vaccine Research Center started. Do you think that devoting substantial resources to a single goal in one center is a strong research model?

PAUL: I think it's a good model.

There is no question that the classical model of individual laboratories with specific research goals that develop as opportunities are pursued is a critical model of inquiry that must persist. But with the growth of technology, new opportunities also arise that can best be capitalized on with the development of single- or limited-purpose entities—centers, if you like—in which technologies can be marshaled in a way that no single laboratory can manage. The VRC is such an example.

I think that NIH as a whole could benefit from having a number of these limited-purpose, highly technological centers—and I think we will see more as a result of the bioterrorism initiatives. I don't think NIH as a whole should be simply made up of these centers, and we must still have a substantial number of programs that retain the free-inquiry model. One other point about this research model is that the centers don't necessarily have to be immortal. They need to exist for as long as their purpose is still valid.

Q: What role do you think the NIH should play in responding to bioterrorism?

PAUL: I think the need to respond to terrorism is rather like the need to respond to HIV. A national emergency arises and a national resource like the NIH has the means and responsibility to respond to it—that is one of the reasons it exists. Within an institution as large and diverse as ours, taking a reasonable chunk and letting it respond to a national emergency is absolutely essential, and we are very well prepared to do it. The resources devoted to the bioterrorism initiative, like the AIDS initiative, have to be proportional to the problem. We have to retain the ability to develop new knowledge that can be the basis of these kinds of focused efforts.

Q: Which of your lifetime achievements are you particularly proud of?

PAUL: I'm proud of a lot of the research that has been done here, and I'm extremely proud of the wonderful colleagues I've had as trainees. Three of my former postdocs are now members of the National Academy of Sciences.

As [do] all scientists who have had long careers, I think about the opportunities missed. The key is to not miss as many in the future. . . .

Lifetime achievement awards imply that you've accomplished all that you are going to—I still feel that there is much more left to do. ■

NIH Research Festival 2002

Plenaries: Biodefense And Bench to Bedside

The 16th Annual NIH Research Festival, the yearly showcase for the NIH intramural research program, will be held **October 15 through 18** in the Natcher Conference Center.

The Research Festival Organizing Committee, co-chaired this year by Barry Hoffer, NIDA scientific director, and Thomas Kindt, NIAID director of intramural research, is now accepting submission of poster abstracts by all NIH staff and Bethesda FDA/CBER staff.

Posters in any area of research conducted by the NIH intramural program will be considered, but the committee is requesting a limit of one poster per first author.

Plenary, mini-symposia, and poster sessions are scheduled on Wednesday and Thursday, October 16 and 17.

There will be two plenary sessions—"Biodefense: A New NIH Mission" and "Bench-to-Bedside: NIH Success Stories" and twelve mini-symposia.

The NIH Job Fair for Postdoctoral Fellows, sponsored by the Office of Education, will kick off the week's events on Tuesday, October 15; the Scientific Equipment Show, sponsored by the Technical Sales Association, will cap them on Thursday and Friday, October 17 and 18, in Parking Lot 10D.

For a preliminary general schedule of events and the online poster registration form, visit the Research Festival website at <**http://festival02.nih.gov**>.

The deadline for **online poster submission** is **5:00 p.m., Friday, August 16**. Applicants will receive e-mail confirmation of receipt of abstracts and will be notified of acceptance by early September.

For more information about poster registration, contact Paula Cohen at (301) 496-1776 or e-mail <**pc68v@nih.gov**>.

Interinstitute Interest Group Directory

Web Access

Note: Although not all the sites are up to date, nearly all the Interest Groups have web sites that can be accessed through the NIH Home Page (<http://www.nih.gov/>) by clicking on "Scientific Resources," then "Special Interest Groups," and then the targeted group(s).

Major Interest Groups

Cell Biology Interest Group
Meeting time: Once every four months
Meeting place: Building 32, Library
Contact: Jennifer Lippincott-Schwartz
Phone: 402-1010; 402-1009
E-mail: <jlippin@helix.nih.gov>
ListServ: subscribe to CELBIO-L

Clinical Research Interest Group
Meeting time and place: sponsors CC Grand Rounds once every other month
Contact: Cliff Lane
Phone: 496-7196
E-mail: <clane@nih.gov>

Genetics Interest Group
Meeting time and place: To be announced: several topic-based symposia will be held
Contact: Dan Kastner
Phone: 496-8364
E-mail: <kastnerd@exchange.nih.gov>
ListServ: subscribe to <GIG-L@list.nih.gov>

Immunology Interest Group
Meeting time: Each Wednesday (except summer), 4:15 pm
Meeting place: Building 10, Lipsett Auditorium
Contact: B. J. Fowlkes
Phone: 301-320-4221
E-mail: <bfowlkes@nih.gov>
ListServ: subscribe to IMMUNI-L by joining the interest group at its web site

Molecular Biology/Biochemistry Interest Group
Meeting time: Yearly to consider speakers
Meeting place: Building 8, Room 122
Contact: Reed Wickner
Phone: 496-3452
E-mail: <wickner@helix.nih.gov>

Neuroscience Interest Group
Meeting time and place: Check website at <http://tango01.cit.nih.gov/sig/home.taf?_function=main&SIGInfo_SIGID=71>
Contact 1: Chip Gerfen
Phone: 496-4341
E-mail: <gerfen@codon.nih.gov>
Contact 2: Betsy Murray
Phone: 496-5625, X-227
E-mail: <eam@ln.nimh.nih.gov>

Structural Biology Interest Group
Meeting time and place: Usually 3rd Tuesday, 4:00 pm, Building 50; notices by e-mail and on the SBIG website: <www.nih.gov/sigs/sbig>
Contact 1: Martin Kessel
Phone: 594-0554
E-mail: <kesselm@mail.nih.gov>
Contact 2: Sandy Markey
Phone: 496-4022
To register for e-mail announcements, join SBIG at <www.nih.gov/sigs/sbig>

Other Interest Groups

AIDS Interest Group
Meeting time and place: Varies
Contact: Fulvia Veronese
Phone: 496-3677
E-mail: <veronesf@od.nih.gov>
ListServ: subscribe to AIDSINTG-L

Apoptosis Interest Group
Meeting time: 1st Monday, 4:00 pm
Meeting place: Building 49, Room 1 50/59 AB
Contact 1: Richard Youle
Phone: 496-6628
E-mail: youle@helix.nih.gov
Contact 2: Yves Pommier
Phone: 496-5944
E-mail: <yp4x@nih.gov>

Behavioral and Social Sciences Interest Group
Meeting time: Varies, in the fall and spring
Meeting place: See NIH Calendar of Events
Contact: Ronald Abeles
Phone: 496-7859
E-mail: <abeles@nih.gov>

Bioethics Interest Group
Meeting time: 1st Monday (except 2nd Monday following holidays; usually does not meet during summer), 3:00 pm
Meeting place: Natcher, Room D, or Building 31, conference room; check yellow sheet or web site
Contact: Miriam Kelty
Phone: 496-9322
E-mail: <mk46u@nih.gov>
Sign up at <http://BIOETHICSinterestgroup@list.nih.gov/>

Biomedical Computing Interest Group
Meeting time: Third Thursday, 3:00 pm
Meeting place: Building 10, Room 2C116 (Medical Board Room)
Contact 1: Jim DeLeo
Phone: 496-3848
E-mail: <jdeleo@nih.gov>
Contact 2: Susan Harris
Phone: 435-8721
ListServe: subscribe to BCIG-L

Biophysics Interest Group
Meeting time and place: Varies (often Building 10, Bunim Room)
Contact: Peter Basser
Phone: 435-1949
E-mail: <pjbasser@helix.nih.gov>

Biosciences Business Interest Group
Meeting time: Monthly, usually during first week; time varies
Meeting place: Varies
Contact 1: Jonathan Sorger
Phone: 496-3208
E-mail: <>
Contact 2: Aniruddho Chaudhuri
Phone: 594-9339

Birth Defects and Teratology Interest Group
Meeting time: Quarterly seminars
Meeting place: Videoconference between Bethesda and Research Triangle Park, N.C.
Contact: Megan Adamson
Phone: 443-4354
E-mail: <madamson@willco.niaaa.nih.gov>

Calcium Interest Group
Meeting time: Usually Tuesday, 3:00 pm
Meeting place: Building 49, Room 1A50
Contact 1: Arthur Sherman
Phone: 496-4325
E-mail: <asherman@nih.gov>
Contact 2: Indu Ambudkar
Phone: 496-1478
ListServ: Subscribe to CALCIUM-L

Cancer CAM Research Interest Group
Meeting time and place: Varies
Contact: Jeffrey White
Phone: 435-7980
E-mail: <jeffreyw@mail.nih.gov>

Chemistry Interest Group
Meeting time: Periodic seminars
Meeting place: Varies
Contact 1: John Schwab
Phone: 594-5560
E-mail: <schwabj@nigms.nih.gov>
Contact 2: Kenneth Kirk
Phone: 496-2619

Chromatin and Chromosomes Interest Group
Meeting time: One Thursday a month, 11:00 am
Meeting place: Building 5, Room 211
Contact: David Clark
Phone: 496-6966
E-mail: <djclark@helix.nih.gov>

Clinical Immunology Interest Group
Meeting time: Monthly, last Wednesday, noon
Meeting place: Building 10, Room 9S235
Contact: Oral Alpan
Phone: 402-3447
E-mail: <oalpan@nih.gov>

Clinical Pharmacology Interest Group
Meeting time: 2-3 times a year in conjunction with special lectures in the NIH Principles of Clinical Pharmacology course, 6:30–7:30 pm
Meeting place: Building 10, Lipsett
Contact: Donna Shields
Phone: 435-6618
E-mail: <dshields@mail.cc.nih.gov>

Cognitive Neuroscience Consortium
Meeting time: Every two months, last Wednesday, 4:15 pm
Meeting place: Building 31, Room 6C10 (starts September 2002; Extramural Program Directors' forum: last Friday every 3rd month, 3:00 pm, NSC Building, Conf. Room 2120, starts October 2002)
Contact: Emmeline Edwards
Phone: 496-9964
E-mail: <ee48r@nih.gov>

Cornea Interest Group
Meeting time: 1st Monday, 8:30 am
Meeting place: Building 6, Room 409
Contact 1: Joram Piatigorsky
Phone: 496-9467
E-mail: <joramp@intra.nei.nih.gov>
Contact 2: Janine Davis
E-mail: <davisj@intra.nei.nih.gov>

Cultural and Qualitative Research Interest Group
Meeting time: 2nd Tuesday, 9:15 am
Meeting place: EPN, room varies
Contact 1: Suzanne Heurtin-Roberts
Phone: 594-6655
E-mail: <sheurtin@mail.nih.gov>
Contact 2: Emeline Otey
Phone: 443-1636 or 3728

Cytokine Interest Group
Meeting time: three to four symposia/year
Meeting place: Varies; one symposium/year at NCI-Frederick
Contact 1: Warren Strober
Phone: 496-6810
E-mail: <wstrober@niaid.nih.gov>
Contact 2: Brian Kelsall
E-mail: <bkelsall@niaid.nih.gov>

Developmental Biology Interest Group
Meeting time and place: Varies
Contact 1: Tom Sargent
Phone: 496-0369
E-mail: <tsargent@nih.gov>
Contact 2: Peggy Zelenka
E-mail: <zelenkap@intra.nei.nih.gov>

DNA Repair Interest Group
Meeting time: 3rd Tuesday, 12:30 pm
Meeting/Videoconference: Natcher, Room H; GRC (Baltimore), Room 1E03; FCRDC, Building 549, Conf. Rm. A; NIEHS (Research Triangle Park, NC) Building 101, Room B200; SUNY, Stony Brook; Univ. of Texas, M.D. Anderson Cancer Center, Smithville, TX; Lawrence Livermore (CA) National Laboratory; Univ. of Michigan, Ann Arbor; Univ. of Kentucky, Lexington; Brookhaven National Laboratory, Upton, NY; Univ. of Pittsburgh
Contact 1: Kenneth Kraemer
Phone: 496-9033
E-mail: <kraemerk@nih.gov>
Contact 2: Vilhelm Bohr
E-mail: <vbohr@nih.gov>

Domestic Violence Research Interest Group
Meeting time and place: To be announced
Contact: John Umhau
Phone: 496-7515
E-mail: <umhau@nih.gov>

Drosophila Interest Group
Meeting time: 3rd Tuesday, 1:15 pm
Meeting place: Building 6B, Room 4B429
Contact 1: Sue Haynes
Phone: 301-295-9791
E-mail: <shaynes@usuhs.mil>
Contact 2: Jim Kennison
E-mail: <kennisoj@exchange.nih.gov>

Drug Discovery Interest Group
Meeting time: Usually one Thursday a month, 3:00 pm
Meeting place: Building 37, 6th-floor conference room
Contact: John N. Weinstein
Phone: 496-9571
E-mail: <weinstein@dtpax2.ncifcrf.gov>

Economics Interest Group
Meeting time and place: Varies
Contact 1: James A. Schuttinga
Phone: 496-2229
E-mail: <js41z@nih.gov>
Contact 2: Agnes Rupp
E-mail: <ar24f@nih.gov>

Endocrinology Interest Group
Meeting time and place: Varies
Contact 1: George Chrousos
Phone: 496-5800
E-mail: <George_Chrousos@nih.gov>
Contact 2: Phil Gold
Phone: 496-1945

End of Life Research Interest Group
Meeting time: Typically Thursdays, 3:00 pm, on an as-needed basis
Meeting place: Natcher, room as available
Contact: Ann Knebel
Phone: 402-6796
E-mail: <aknebel@nih.gov>

Epidemiology and Clinical Trials Interest Group
Meeting time and place: Varies (subscribe to ListServ for notices)
Contact: Martina Vogel-Taylor
Phone: 496-6614
E-mail: <martinav@nih.gov>
ListServ: subscribe to Epidem-L at <listserv@list.nih.gov>

Fluorescence Interest Group
Meeting time: Usually even Fridays, 4:00 pm; see website
Meeting place: Building 10, usually Room 5N264
Contact: Jay Knutson
Phone: 496-2557
E-mail: <jaysan@helix.nih.gov>
Contact 2: Dan Sackett
E-mail: <sackettd@mail.nih.gov>

Gene Therapy Interest Group
Meeting time: 2nd Thursday, 2:00 pm
Meeting place: Building 10, Lipsett Auditorium
Contact: Fabio Candotti
Phone: 402-1833
E-mail: <fabio@nhgri.nih.gov>

Interinstitute Interest Group Directory

Genomics and Bioinformatics Interest Group
Meeting time: Usually one Thursday a month, 3:00 pm
Meeting place: Building 37, 6th-floor conference room
Contact: John N. Weinstein
Phone: 496-9571
E-mail: <weinstein@dtpax2.ncifcrf.gov>

Glycobiology Interest Group
Meeting time and place: Varies
Contact: Diana Blithe
Phone: 435-6990.
E-mail: <blithed@nih.gov>
ListServ: Subscribe to GLYCO-L@LIST.NIH.GOV

GTP Binding Proteins Interest Group
Meeting time: Irregular
Meeting place: FAES Social & Academic Ctr.
Contact: R. Victor Rebois
Phone: 496-2007
E-mail: <reboisv@ninds.nih.gov>

Hard Tissue Disorders Interest Group
Meeting time: Day varies, 9:30 am
Meeting place: Building 30, Room 117
Contact: Pamela Robey
Phone: 496-4563
E-mail: <probey@dir.nidcr.nih.gov>
Contact 2: Michael Collins
Phone: 496-4913

Head and Neck Cancer Interest Group
Meeting time: To be announced
Meeting place: Building 30, Room 117
Contact 1: Adrian Senderowicz
Phone: 594-5270
E-mail: <adrian.senderowicz@nih.gov>
Contact 2: Wendy Weinberg
Phone: 301-827-0709
E-mail: <weinberg@cber.fda.gov>

History of Biomedical Research Interest Group
Meeting time: Second Tuesday, 3:30 pm
Meeting place: Varies; check web site
Contact 1: NIH History Office
Phone: 496-6610
Contact 2: Victoria Harden
E-mail: <hardenv@od.nih.gov>

Image Processing Interest Group
Meeting time and place: Distributed by e-mail and on <image.nih.gov>
Contact 1: Benes Trus
Phone: 496-2250
E-mail: <trus@helix.nih.gov>
Contact 2: Matt McAuliffe
Phone: 594-2432

Imaging Ligand Development Consortium
Meeting time and place: To be announced (every 3 months; steering committee meetings will be held every 2 months in the Neuroscience Center)
Contact: Linda Brady
Phone: 443-5288
E-mail: <LB@helix.nih.gov>

Integrative Neuroscience Interest Group
Meeting time: Alternate Thursdays, 4:00 pm
Meeting Place: Building 49, Room 1A51
Contact: Betsy Murray
Phone: 496-5625, X-227
E-mail: <eam@ln.nimh.nih.gov>

In Vivo NMR Interest Group
Meeting time: Varies
Meeting place: Building 10, Room B1N256
Contact: Jeff Duyn
Phone: 594-7305
E-mail: <jhd@helix.nih.gov>

Java Interest Group
Meeting time and place: Announced through ListServe; join at <list.nih.gov/archives/java.html>
Contact 1: John Ostuni
Phone: 451-9935
E-mail: <ostuni@helix.nih.gov
Contact 2: Jai Evans
E-mail: <evansj@helix.nih.gov>

Knowledge Management Interest Group
Meeting time: 4th Wednesday, 2:30 PM (changes will be noted on NIH Calendar and KMIG website)
Meeting place: Wolff Conference Room, Building 10, Room 11S235
Contact 1: Geoffrey Marsh
Phone: 301-594-9683
E-mail: <geoff@mail.nih.gov>
Contact 2: Paul Beatty
E-mail: <pbeatty@mail.nih.gov>

Lambda Lunch (Bacterial and Phage Genetics)
Meeting time: Each Thursday, 11:00 am
Meeting place: Building 36, Room 1B13
Contact: Susan Gottesman
Phone: 496-3524
E-mail: <susang@helix.nih.gov>
Anonymous FTP site:FTP.CU.NIH.-GOV
directory "LAMBDA_LUNCH"

Light Microscopy Interest Group
Meeting time: Monthly, Tuesday, noon
Meeting place: Building 10, Room 4B51
Contact: James McNally
Phone: 402-0209
E-mail: <mcnallyj@mail.nih.gov>
Contact 2: Christian Combs
Phone: 496-0014

Lymphoma and Leukemia Interest Group
Meeting time: Varies
Meeting place: Building 10, Room 12S235a
Contact: Michael Bishop
Phone: 435-2764
E-mail: <mbishop@mail.nih.gov>
ListServ: LLig-1

Mass Spectrometry Interest Group
Meeting time: 1st & 3rd Thursday, 10:30 am
Meeting place: Building 10, Room 7C101
Contact: Lewis Pannell
Phone: 402-2196
E-mail: <L_Pannell@nih.gov>

Membrane Microdomains Interest Group
Meeting time: 1st Tuesday, 12:00 noon
Meeting place: Building 10, Room 9C209
Contact: Teresa Jones
Phone: 496-8711
E-mail: <tlzj@helix.nih.gov>

Membrane Protein Interest Group
Meeting time: Monthly, usually Wednesday, 1:00 pm; check website
Meeting place: Building 5, Room 127
Contact: Reinhard Grisshammer
E-mail: <rkgriss@helix.nih.gov>

Microarray Users Group
Meeting time and place: Varies
Contact: Katherine Peterson
Phone: 402-6537
E-mail: <petersonk@nei.nih.gov>

Mitochondria Interest Group
Meeting time: 1st Monday, 3:00 pm
Meeting/Videoconference: Natcher, Room H; NIEHS, Research Triangle Park, NC; GRC, Baltimore; UC Davis; Univ. of Maryland, Baltimore; Admin. Bldg, Room B113, NIST, Gaithersburg, MD; VA Hospital, Cleveland; Podell Auditorium, Beth Israel Medical Center, NYC
Contact: Steve Zullo
Phone: 301-975-8984
E-mail: <zullo@nist.gov>
Contact 2: Mariana Gerschenson
E-mail: GerscheM@nhlbi.nih.gov

Molecular Modeling Interest Group
Meeting time: See <http://mmignet.nih.gov>
Meeting place: Building 12A, conf. rooms
Contact: Peter Steinbach
Phone: 496-1100
E-mail: <steinbac@helix.nih.gov>

Molecular Recognition and Quantitative Interaction Interest Group
Meeting time: 1st Wednesday, 5:30 pm
Meeting place: Building 6A, Room 4A05
Contact: Robert Crouch
Phone: 496-4082
E-mail: <robert_crouch@nih.gov>

Motility Interest Group
Meeting time and place: Varies
Contact: Jim Sellers
Phone: 496-6887
E-mail: <sellersj@nhlbi.nih.gov>

Mouse Club
Meeting time: 1st Tuesday, 4:00 pm
Meeting place: Building 6A, Room 4A05
Contact: Heiner Westphal
Phone: 402-0545
E-mail: <hw@helix.nih.gov>

Muscle Interest Group
Meeting time: Alternate Thursdays, noon
Meeting place: Building 40, Room 1203/1205
Contact 1: Andres Buonanno
Phone: 496-0170
E-mail: <buonanno@helix.nih.gov>

Mycobacterial Interest Group
Meeting time: To be announced
Meeting place: Building 29, Room 121, or Twinbrook II, 2nd-floor conference room
Contact 1: Clifton Barry
Phone: 435-7509
E-mail: <cbarry@niaid.nih.gov>
Contact 2: Mike Brennan
Phone: 496-9559

Neural-Immune Interactions Interest Group
Meeting time and place: To be announced
Contact: Socorro Vigil-Scott
Phone: 496-9255
E-mail: <vigilscs@intra.nimh.nih.gov>

Neurobiology Interest Group
Meeting time: alternate Fridays, 4:30 pm
Meeting place: Cloisters, Rathskeller
<http://tango01.cit.nih.gov/sig/home.taf?_function=main&SIGInfo_SIGID=71>
Contact: Chip Gerfen
Phone: 496-4341
E-mail: <gerfen@helix.nih.gov>
ListServ: <http://intra.ninds.nih.gov/nig/>

Neuroinformatics Interest Group
Meeting time: 2nd Tuesday, 12:00 noon
Meeting place: Building 49, Conference Room 1A/B
Contact 1: Yuan Liu
E-mail: <liuyuan2@ninds.nih.gov>
Phone: 496-1917
Contact 2: Barry Davis
Phone: 402-3464

PET Interest Group
Meeting time: Each Friday, 2:00 pm
Meeting place: Building 10, Room 1C520
Contact: Peter Herscovitch
Phone: 402-4297
E-mail: <herscovitch@nih.gov>

Phage-Tech Interest Group
Meeting time and place: Varies
Contact 1: Dean Scholl
E-mail: <dscholl@usa.net>
Contact 2: Carl Merril
Phone: 435-3583

Pigment Cell Research Interest Group
Meeting time: 3rd Monday, 3:00 pm
Meeting place: Building 49, 1st-floor Conference Room
Contact 1: Bill Pavan
Phone: 496-7584
E-mail: <bpavan@nhgri.nih.gov>
Contact 2: Vincent Hearing
Phone: 496-1564

Polyunsaturated Lipid Function Interest Group
Meeting time: Usually 1st Wednesday of each month (journal club; resuming in September), 1:00 pm
Meeting place: Flow Bldg. Conference Room, Rockville, 12501 Washington Ave.
Contact: Norman Salem
Phone: 443-2393
E-mail: <nsalem@niaaa.nih.gov>

Prostate Cancer Interest Group
Meeting time: 2nd & 4th Tuesdays, 4:00 pm
Meeting place: Building 10, Room 2S235
Contact: Kathleen Simon
Phone: 496-6353
E-mail: <simonk@mail.nih.gov>

Protein Trafficking Interest Group
Meeting time: 2nd Tuesday, 3:30 pm
Meeting place: Building 10, Room 9S235
Contact 1: Harris Bernstein
Phone: 402-4770
E-mail: <harris_bernstein@nih.gov>
Contact 2: Peng Loh
Phone: 496-3239

Proteomics Interest Group
Meeting time and place: Monthly seminars, check website: <http://proteome.nih.gov>
Contact: Donita Garland
Phone: 496-6999
E-mail: <dgarland@helix.nih.gov>

Reactive Oxygen Species Interest Group
Meeting time and place: Monthly seminars with Oxygen Club of the Greater Washington Area (info via NIH Calendar, members' e-mail, and <henry.rodriguez@nist.gov>)
Contact 1: Mike Chiueh
Phone: 496-3421
E-mail: <chiueh@helix.nih.gov>
Contact 2: Mike Espey
Phone: 496-7511

RNA Club
Meeting time: 1st Tuesday (except August), 4:00 pm
Meeting place: Building 41, Room C509
Contact 1: Carl Baker
Phone: 496-2078
E-mail: <ccb@nih.gov>
Contact 2: Susan Haynes
E-mail: <shaynes@usuhs.mil>

Signal Transduction Interest Group
Meeting time: Alternate Fridays, 4:30 pm
Meeting place: 5 Research Court, Room 2A08
Contact 1: John Northup
Phone: 496-9167
E-mail: <drjohn@codon.nih.gov>
Contact 2: James Battey
Phone: 402-0900

Stem Cell Interest Group
Meeting time and place: TBA; check website
Contact 1: Peter Gasper
Phone: 1-410-558-8260
E-mail: <gasperpe@grc.nia.nih.gov>
Contact 2: Kevin Becker
E-mail: <beckerk@grc.nia.nih.gov>

Stroke Branch Interest Group/Seminar
Meeting time: Thursdays 3:30 pm
Meeting place: Building 36, Conf. Room 1B13
Contact 1: John Kylan Lynch
Phone: 496-1187/1714
E-mail: <LynchJ@ninds.nih.gov>
Contact 2: Zurab Nadareishvili
Phone: 496-6231

Synaptic and Developmental Plasticity Interest Group
Meeting time: Wednesday, 12:00 noon
Meeting place: Building 49, Room 1A50
Contact: Bai Lu
Phone: 435-2970
E-mail: <lub@codon.nih.gov>

Interinstitute Interest Group Directory

Therapeutic Oligonucleotides Interest Group
Meeting time: Last Thursday, 4:00 pm
Meeting place: Building 10, Room 2C116
Contact : Yoon Cho-Chung,
Phone: 496-4020
E-mail: <chochung@helix.nih.gov>

Transcription Factors Interest Group
Meeting time: 1st Thursday (except July-Sept.), 1:30 pm
Meeting place: Building 49, Conference Room B
Contact 1: Stoney Simons
Phone: 496-6796
E-mail: <steroids@helix.nih.gov>
Contact 2: Uli Siebenlist
Phone 496-8917
ListServ: subscribe to TFACTORS

Tumor Angiogenesis & Invasion Working Group
Meeting time and place: Posted at web site
Contact 1: William Figg
Phone: 402-3622
E-mail: <wdfigg@helix.nih.gov>
Contact 2: Steven Libutti
Phone: 496-5049

Veterinary Interest Group
Meeting time: 3rd Thursday, 12:00 noon
Meeting place: Varies
Contact: Kay Jordan
Phone: 402-4547
E-mail: <ekj@helix.nih.gov>

Viral Hepatitis Interest Group
Meeting time: One Monday a month, 3:30 pm
Meeting place: Building 10, 9S235 (Bunim)
Contact: Marian Major
Phone: 301-827-1881
E-mail: <major@cber.fda.gov>

Virology Interest Group
Meeting time: 3rd or 4th Tuesday, 12:15 p.m.; minisymposium in November
Meeting place: Building 4, Room 433
Contact 1: Alison McBride
Phone: 496-1370
E-mail: <amcbride@niaid.nih.gov>
Contact 2: Kathryn Carbone
E-mail: <carbonek@cber.fda.gov>
ListServ: Contact <CBuckler@nih.gov>

Washington Area Yeast Club
Meeting time: 2nd Wednesday, 4:30 pm
Meeting place: Building 6A, Room 4A05
Contact 1: Reed Wickner
Phone: 496-3452
E-mail: <wickner@helix.nih.gov>
Contact 2: Alan Hinnebusch
Phone: 496-4480
E-mail: <ahinnebusch@nih.gov>

Women's Reproductive Health Interest Group
Meeting time and place: Every 4 months at times decided by the group.
Contact: Phyllis Leppert
Phone: 496-6515
E-mail: <leppertp@mail.nih.gov>

WorldWideWeb Interest Group
Meeting time: 2nd Tuesday every other month, 9:30 am
Meeting place: Building 50, Conference Room
Contact 1: Sandy Desautels
Phone: 402-6553
E-mail: <sandy_desautels@nih.gov>
Contact 2: Dale Graham
E-mail: <degraham@helix.nih.gov>

Xenopus/Zebrafish Interest Group
Meeting time: Last Monday (except summer), 3:30 pm
Meeting place: Building 6B, Room 429
Contact 1: Brant Weinstein
Phone: 435-5760
E-mail: <bw96w@nih.gov>
Contact 2: Ajay Chitnis
E-mail: <chitnisa@mail.nih.gov>

X-ray Crystallography Interest Group
Meeting time: Quarterly, announced by e-mail, 2:00 pm
Meeting place: Building 5, Room 127
Contact: Xinhua Ji
Phone: (301) 846-5035
E-mail: <jix@ncifcrf.gov>

Addenda

Considering starting a new Interest Group? Contact* Celia Hooper *(fax: 301-402-4303; e-mail: <hooperc@od.nih.gov>.

Need to correct your group's listing? Contact CIT's web publishing group: <publish@cit.nih.gov>.

Online Technology Transfer Training

Over the years, NIH intramural research scientists have been actively involved in all aspects of technology transfer. To date, more than 500 Cooperative Research and Development Agreements (CRADAs) and thousands of material transfer agreements (MTAs) have been signed. Additionally, more than 1,500 license agreements have been executed. These collaborations and exchanges have generated a wealth of technologies, including new therapeutic drugs, materials, methods, and devices that have improved the public health.

To help educate scientists about technology transfer, NIH has launched the NIH On-Line Technology Transfer Training course. Major areas addressed include MTAs, CRADAs, patents and inventions, licensing, royalties, and ethics. Click on

<http://tttraining.od.nih.gov>.

This one time, 40-minute training is required for senior investigators, senior scientists/clinicians, investigators, and adjunct investigators. An abbreviated course is required for fellows, staff scientists/clinicians, and graduate students. The site can be used as an online reference tool on technology transfer for anyone interested.

Although originally designed for NIH intramural scientists, the training is also useful for anyone who wants or needs to know more about technology transfer, such as laboratory and administrative staff. ■

Cancer Detection Bioinformatics

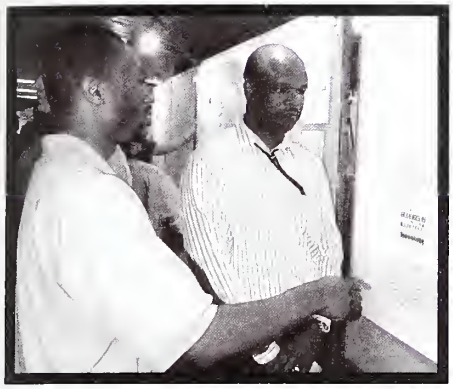
The NCI Division of Cancer Prevention (DCP) is holding a workshop on Bioinformatics in Cancer Detection August 6 and 7, Natcher Auditorium. Eric Lander of the Whitehead Institute, Cambridge, Mass., will give the keynote. The list of invitees includes more than 20 experts in bioinformatics of genomics, proteomics, multifactorial, biomarker analysis, and pattern recognition. The goal of the workshop is to determine how bioinformatics may be used in the early detection, risk assessment, and risk reduction of cancer. To register online, go to

<http://cancer.gov/prevention/abcd>.

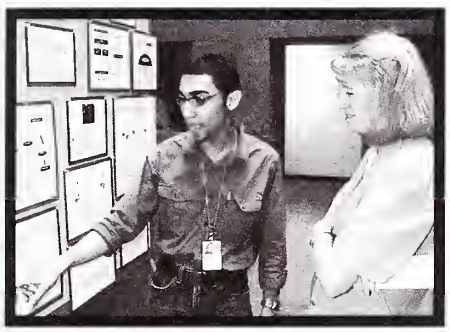
For more information, contact Robert Negm at 301-435-5015. ■

Postbac Poster day

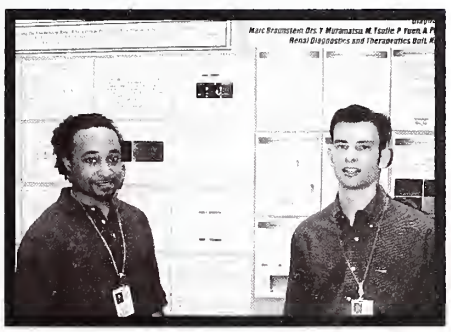
On May 8th, students doing research at 15 institutes and the Clinical Center presented 161 posters to the NIH community. OE's Valerie McCaffrey was on hand to capture the occasion.



(left) ***Ekinadese Aburime****, Clark Atlanta University, with Alfred Johnson, Office of Loan Repayment and Scholarship. Poster: "Potentiation of TGF-β effects on gene induction in fibroblasts by ionizing radiation" (preceptors: Anita Roberts and Kathleen Flanders, NCI Laboratory of Cell Regulation and Carcinogenesis)*



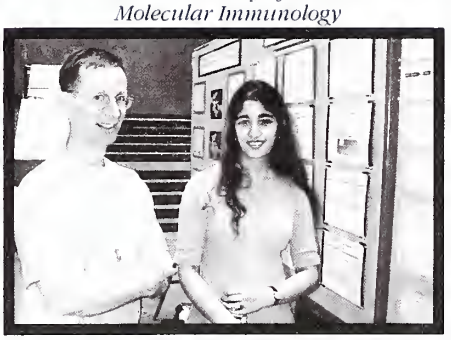
Emerito Amaro-Carambot*, University of Puerto Rico, Humacao, with preceptor B. J. Fowlkes, NIAID Laboratory of Cellular and Molecular Immunology. Poster: "The Role of* notch *in T-cell development: An in vivo experimental evaluation"*



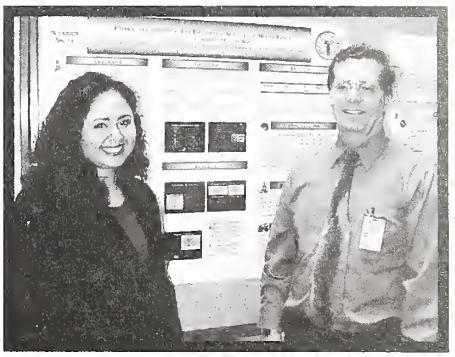
(left): ***Brent Elliott****, George Mason University (Fairfax, VA), "Investigating the biochemical role of nicastrin in presenillin function in* Dictyostelium discodeum *(preceptor: Alan Kimmel, NIDDK Laboratory of Cellular and Developmental Biology); (right):* ***Marc Braunstein****, CUNY Brooklyn College, "Diagnosis of acute renal failure" (preceptor: Robert Star, NIDDK Metabolic Diseases Branch)*

(left): ***Tiffany Adams****, Virginia Union University, Richmond, "A cellular mechanism for the processing and sorting of proinsulin: implication for familial hyperinsulinemia (preceptors: Y. Peng Loh and Savita Dhanvantari, NICHD Laboratory of Developmental Neurobiology); (right):* ***Noelia Rodriguez****, University of Puerto Rico, Cayey, "Identification and characterization of an epidermal differentiation-specific gene" (preceptor: Maria Morasso, NIAMS Laboratory of Skin Biology)*

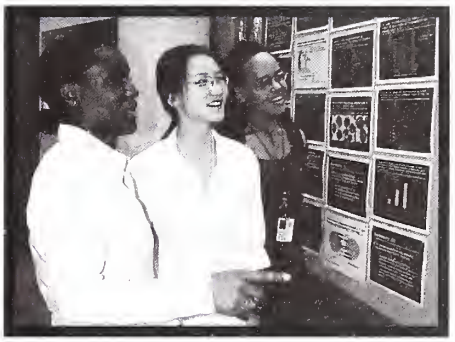
(left to right): Debbie Cohen, OE, ***Kristen Stover****, Pennsylvania State University, University Park, "Spectral karyotyping (SKY) of a panel of human cancer cell lines used in a drug-discovery screen by the National Cancer Institute" (preceptor: Ilan Kirsch, NCI Medicine Branch, Department of Genetics); and* ***Jason Drury****, Northwestern University (Evanston, IL), "Viral vector applications using a thymic stromal cell-type-specific promoter" (preceptor: Moon Kim, NIAID Laboratory of Cellular and Molecular Immunology*



Ipsita Mukherjee*, University of Maryland, College Park, with Karl Pfeifer, NICHD. Poster: "Determining the inheritance pattern of a knockout allele of the La antigen" (preceptor: Richard Maraia, NICHD Laboratory of Molecular Growth Regulation)*



Nora Vasquez*, University of Washington (Seattle), with her lab chief Harry Malech. Poster: "Enzymatic characterization of mouse eosinophil-associated ribonuclease 1" (preceptors: Helene Rosenberg and Kim Dyer, NIAID Laboratory of Host Defenses)*



(left to right): ***Joanne Moreau****, New York University, "Differential expression of mouse ribonucleases in response to challenge with viral pathogens" (preceptor: Helene Rosenberg, NIAID Laboraory of Host Defenses);* ***InHye Cho****, a NIAID postbac; and* ***Kisani Ogwaro****, San Diego State University, "Defects in CD4+ T-cell-mediated B-cell help in HIV-infected patients" (preceptors: Susan Moir and Anthony Fauci, NIAID Laboratory of Immunoregulation)*

(left to right): ***Andrea Hoberman****, Cornell University, Itbaca, NY), "Performance on an affect identification task in children and adults" (done with* ***Alison Merikangas****, Carnegie Mellon University, Pittsburgh; preceptor: Daniel Pine, NIMH Mood and Anxiety Disorder Research Program);* ***Guy Manetti****, University of Pennsylvania, Philadelphia, "Increased cerebrospinal fluid levelsof IL-1, IL-6, and IL-10 in patients with dementia of the Alzheimer's type" (preceptors: Trey Sunderland and Nadeem Mirza, NIMH Geriatric Psychiatry Branch); and* ***Thalia Margalit****, Dartmouth College, Hanover, NH, "Bebavioral response to affective stimuli by bipolar children" (preceptor: Ellen Leibenluft, NIMH Pediatric and Developmental Neuropsychiatry Branch)*

Recently Tenured

Julie Donaldson *received her Ph.D. from the University of Maryland, Baltimore, in 1988 and did postdoctoral work at NICHD before joining the Laboratory of Cell Biology of NHLBI in 1995. She is now a senior investigator in the Laboratory of Cell Biology, NHLBI.*

Fran Pollner

Julie Donaldson

My research interests are in the organization of membrane compartments in cells. Membrane-bound organelles carry out distinct biochemical functions in eukaryotic cells. Understanding how these organelles maintain their properties and communicate with and transfer materials to other organelles is a fascinating area in cell biology, referred to as membrane traffic.

Over the past six years, my laboratory has focused on membrane traffic during endocytosis, in which plasma membrane proteins, receptors, and extracellular materials are brought into the cell as vesicles. The most studied and best understood type of endocytosis is clathrin-mediated endocytosis in the selective uptake of specific receptors and ligands into cells.

By contrast, very little is known about the various clathrin-independent forms of endocytosis. These alternative endocytic mechanisms are important as modes of entry for certain toxins, bacteria, and viruses and for the plasma membrane reorganization that accompanies phagocytosis, tissue differentiation, and cell migration.

We began to characterize a novel clathrin-independent endocytosis pathway through our studies on Arf6, a low-molecular-weight GTP-binding protein (GTPase). GTPases function as molecular switches, in the active form when GTP is bound and in the inactive form when GDP is bound after GTP hydrolysis. The Arfs comprise a family of proteins related to the Ras superfamily of GTPase regulators.

While I was a postdoctoral fellow in NICHD, I studied the role of Arf1 in regulating membrane traffic and organelle structure at the Golgi complex, a processing and sorting station for secretory proteins after they have left the endoplasmic reticulum. Then, as an independent investigator, my colleagues and I began studying Arf6 and found that this Arf localizes to the plasma membrane and to endosomal membranes that are distinct in protein and lipid composition from those endosomes derived from the clathrin-mediated endocytic pathway.

Among the proteins that travel along this endocytic pathway are important immunologic proteins such as the MHC Class I proteins and proteins associated with cell adhesion such as the integrins. We showed that Arf6, through its cycle of activation and inactivation, regulates the movement of membrane through this endosomal system. After internalization, a fraction of this membrane is recycled back to the plasma membrane in an Arf6-dependent manner, and another fraction of this membrane fuses with membrane internalized via the clathrin pathway. Thus, this Arf6-associated endosomal membrane system parallels and intersects with the clathrin pathway.

An interesting feature of Arf6 is that in addition to regulating membrane trafficking, it also regulates the actin cytoskeleton underlying the plasma membrane. We discovered several years ago that acute activation of Arf6 results in the formation of cell surface protrusions that are enriched in actin filaments. Furthermore, we found that the Rac GTPase implicated in plasma membrane ruffling and cell migration associates with the Arf6 endosome and that Rac's ability to form membrane ruffles is dependent upon Arf6 function.

Fran Pollner

Gerhard Hummer

The finding that an Arf family member could regulate the actin cytoskeleton surprised researchers in the actin cytoskeletal field. This result was later corroborated by my group and others in demonstrating an Arf6 requirement for other actin-dependent processes such as cell spreading, Fc-mediated phagocytosis, and cell migration.

A key question for my lab is how Arf6 functions to affect both membrane traffic and the actin cytoskeleton. One important feature of Arfs is their ability to alter membrane lipid composition. We found that Arf6, through its regulation of a phosphatidylinositol kinase, modulates phosphatidylinositol 4,5-bisphosphate levels at the plasma membrane and on the Arf6-associated endosomes influencing membrane traffic and actin structures at the surface.

The roles played by membrane lipids in membrane trafficking pathways is now an area of intense research in my lab and in many others. We are also interested in identifying regulators of Arf6, identifying other proteins that travel through the Arf6 pathway, and understanding the molecular details of how membrane traffic is regulated in endocytic membrane systems.

Gerhard Hummer *did his graduate studies at the Max-Planck-Institute for Biophysical Chemistry in Goettingen, Germany, and at the University of Vienna, Austria, where he received his Ph.D. in 1992. He then moved to the Los Alamos National Laboratory as a postdoctoral fellow and became a principal investigator in 1996. He joined NIH in 1999 and is now a senior investigator in the Laboratory of Chemical Physics, NIDDK.*

My interests are in the area of biomolecular structure, dynamics, and function, with a focus on solvent effects studied by theory and computer simulations.

Water penetration into proteins and transient fluctuations in hydration in the interior of proteins are important to their stability and function. Water-mediated proton transfer, in particular, is fundamental to bioenergetics and enzyme catalysis. An important goal driving my research at NIDDK is to understand how nonpolar channels function in protein-mediated proton transfer.

From computational studies of simple model channels, we found that single-file chains of water molecules can fill narrow molecular pores even if the hydrophobicity of the pore walls causes substantial losses of hydrogen-bonding energy. Water filling and emptying of hydrophobic channels can be regulated by small changes in channel polarity. In proteins such as cytochrome C oxidase, bacteriorhodopsin, and cytochrome C P450, the observed sensitivity to polarity can provide a tight coupling of water-mediated proton delivery to electron transfer and active-site chemistry.

This polarity-controlled filling and emptying of channels can help in particular to prevent proton leakage and unwanted side reactions by "dissolving" the proton wire after a successful proton transfer.

My lab's studies also shed new light on the mechanism of rapid water conduction through biological water pores. In our simulations of nonpolar channels, we observed pulselike transport of water with an average flow rate comparable to that measured for a biological water channel, aquaporin-1.

Indeed, structures of aquaporin-1 show that relatively nonpolar residues line much of the pore. For optimal water transport, the polarity of the pore needs to be sufficiently high to ensure water filling, but low enough not to hinder water motion by strong directional interactions. Increased polarity would only slightly enhance the water occupancy but would greatly reduce the water mobility.

In cytochrome C oxidase, a proton pump in the respiratory chain, my collaborators and I have studied the side-chain and hydration dynamics of the active-site region. Solvent sites, identified through computation, establish a continuous proton path from the membrane inside to a critical glutamic acid residue. Our calculations further suggest that the glutamic acid shuttles a proton into the hydrophobic active-site cavity, to be picked up by transient water molecules. A combination of experiment, theory, and simulation allowed us to put important constraints on the proton pumping mechanism of cytochrome C oxidase.

My group is also working on fundamental aspects of the hydrophobic effect, in particular its role in ligand binding and protein folding. Other work with colleagues is leading to theories for single-molecule experiments. These are applied to nonequilibrium single-molecule pulling by atomic-force microscopes and laser tweezers, for example, to extract equilibrium thermodynamic properties, such as binding constants.

In future work, we will build on this understanding of nonequilibrium processes and proton delivery mechanisms to understand how cytochrome C oxidase converts energy and acts as a "Maxwell demon" by pumping protons across membranes against an electrostatic potential and chemical gradient. ■

New Cancer Research Fellowship For Women Scientists Won by Best

The NCI Fellowship Office has announced the opening of the first national competition for the Sallie Rosen Kaplan Fellowship, an award sponsored by the Foundation for the NIH to support women postdoctoral scientists in cancer research. Carolyn Best, the first recipient of the award (made this year to extend the work of a current postdoc), describes below the research she's been involved in and the work the fellowship will enable her to continue.

Bill Branson

Carolyn Best began her fourth postdoc year this July with the help of the Sallie Rosen Kaplan Fellowship. The first recipient of the new award, Best works in the Pathogenetics Unit (chief, Michael Emmert-Buck) of the NCI Laboratory of Pathology (chief, Lance Liotta)

Research Focus

We are investigating the gene expression changes that occur during human prostate cancer progression. The technology of cDNA microarrays allows for the simultaneous measurement of the expression levels of tens of thousands of genes, and we have been able to identify groups of genes whose expression changes as prostate cancer progresses from early to more advanced stages.

For example, the majority of men diagnosed with prostate cancer have moderate-grade tumors with an uncertain prognosis. Most of these men will do well with conservative treatment; however, a significant percentage of these tumors will behave as though they were high-grade—they will quickly metastasize. We have identified numerous genes that differ significantly in tumors and normal tissue and have developed a profile of 21 genes that differentiate high-grade from moderate-grade prostate cancer. These data provide important insight into prostate tumorigenesis and may have clinical utility in the identification of key molecular features of aggressive cancer.

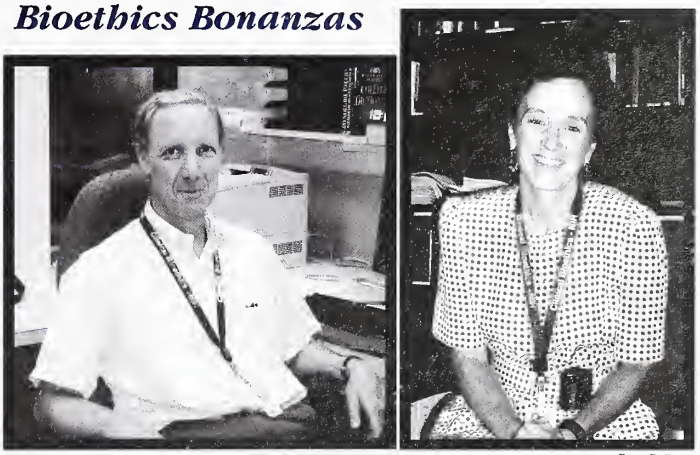
Continuing Research

One of our highest priorities is following up on the expression-profiling data generated thus far. For example, the 21 candidate genes that may be able to differentiate high- and moderate-grade prostate cancer must be validated in a much larger number of cases and using different technological methods. In addition, our initial expression-profiling effort has resulted in several new collaborations to verify our findings both technically and biologically.

—Carolyn Best

*The deadline for applications and supporting letters in the first national competition is **February 1, 2003**, for postdoctoral fellowships beginning in July 2003. Selected candidates will be notified May 1, 2003. For application criteria and instructions to apply online (strongly encouraged) or by mail, contact Lee McPhatter at 301-496-4796 (fax: (301) 451-6238, e-mail: **<lm148g@nih.gov>**). For additional information, see also the NCI Fellowship Office website:**<http://www.nci.nih.gov/fellowships>http://www.nci.nih.gov/fellowships>**.*

Bioethics Bonanzas



Fran Pollner

Franklin Miller (far left), a special expert in the CC Department of Clinical Bioethics, and Christine Grady, head of the Department's Section on Human Subjects Research, have been elected Fellows of the Hastings Center—the "bioethicist equivalent of the National Academy," says Department chief Ezekiel Emanuel.

Call for Catalytic Reactions

In this issue, we are asking for your reactions in four areas: knowledge gaps, Interest Groups as catalysts, responding to national emergencies, and *Catalyst* content.

Send your responses on these topics or your comments on other intramural research concerns to us via e-mail: <catalyst@nih.gov>; fax:402-4303; or mail: Building 2, Room 2W23.

In Future Issues...

- New Clinical Center Research Tools
- Bioinformatics' Grimmest Task
- Cetting a GRIP On Global Health

1) NIH's new director has challenged NIH investigators to identify key knowledge gaps that block the advance of biomedical science. What do you see as the one most important unanswered question in biomedical research today?

2) How can the NIH Special Interest Groups be utilized more effectively to advance the NIH science agenda?

3) How can NIH resources best be used in responding to precipitous national events such as the threat of bioterrorism?

4) What features of the *Catalyst* do you most appreciate? What issues would you like to see covered—or not covered?

The NIH Catalyst is published bi-monthly for and by the intramural scientists at NIH. Address correspondence to Building 2, Room 2W23, NIH, Bethesda, MD 20892. Ph: (301) 402-1449; fax: (301) 402-4303; e-mail: <catalyst@nih.gov>

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